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Case presentation

Blue rubber bleb nevus syndrome: a rare multisystem affliction

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Abstract

About 200 cases of blue rubber bleb nevus syndrome (BRBNS) have been reported in the literature. The disorder affects both sexes equally and the occurrence is mostly sporadic except for a few reports of cases with autosomal dominant inheritance pattern. Herein we report an 11-year-old girl with progressive BRBNS and onset at 5 years of age.

Introduction

Blue rubber bleb nevus syndrome (BRBNS) is a rare disorder characterized by cutaneous and gastrointestinal venous malformations [1]. The association between cutaneous and visceral hemangiomas and gastrointestinal bleeding was first described by Gascoyen in 1860, in a patient having multiple hemangiomas of skin, GI tract, and parotid gland with severe anemia [2].

In 1958, William Benett Bean [3] further gave the detailed description of the condition and coined the term blue rubber bleb nevus syndrome (BRBNS), which exhibits three patterns of skin lesions; (a) multiple easily compressible protuberant blood filled sacs, (b) pleomorphic flat blue lesions, with occasional black stippling, that merges with adjacent normal skin, (c) large hemangiomas that may lead to obstruction of the airway, alimentary canal, or other vital structures.

About 200 cases of BRBNS have been reported in literature.. The disorder affects both sexes equally and the occurrence is mostly sporadic except a few reports of cases with autosomal dominant inheritance pattern [4]. The cause of this syndrome is unknown [5], and it has not been attributed to any specific gene or chromosome [6]. However, some studies have suggested that the gene located on chromosome 9, responsible for autosomal dominantly inherited familial venous malformations, might be the culprit in BRBNS as well [7].

Keywords: Blue rubber bleb nevus syndrome, cutaneous venous malformation, gastrointestinal bleeding

Case synopsis

An 11-year-old girl presented to the outpatient department of dermatology with a history of blue colored lesions on her right chest and upper back since the age of 5 years, progressively increasing in size since then. The patient had been experiencing recurrent nocturnal episodes of pain in the lesions for 6 months prior to presentation. There was no history of associated hyperhidrosis over the lesions.

The patient did not have any complaints like melena, hematemesis, headache, bone pains, or visible bony deformities suggestive of malformations in other visceral organs, but she did complaint of a generalized feeling of weakness and malaise. Her mother denied any history of similar lesions in other family members.

On physical examination, multiple variably sized bluish purple colored nodules were present on the right anterolateral chest region with bluish flat macular lesions of varying size on adjoining skin over right chest, extending up to the back. The lesions produced focal contour bulges on the right chest leading to thoracic asymmetry.

The largest nodule was 4.4 x 3.5 cm in size with a soft elevated nipple like center and a rubbery feel on palpation. It was compressible with near total emptying on application of firm pressure.

The flat blue-colored macules, extending from the right anterolateral chest to the upper back, blanched partially on pressure and gave the skin over this region a mottled blue appearance.



Figure 1. Nodular bluish purple compressible sacs with nipple like protuberance and rubbery feel on palpation **Figure 2.** Lateral view right chest shows extent of lesions. Both nodular and bluish macular lesions are visible

A complete hemogram revealed microcytic hypochromic anemia. Leukocyte and platelet counts, coagulation profile, and urinalysis were within normal limits.

The stool examination for occult blood loss was positive on two separate occasions, suggesting a possibility of gastrointestinal lesions.

Magnetic Resonance Imaging of affected regions revealed multiple lobulated masses of closely clustered tortuous serpiginous vessels over the right hemithorax anteriorly, laterally, and posteriorly, involving cutaneous and subcutaneous tissues along with latissimus dorsi, serratus anterior, and intercostal muscles. There was no intraosseous or intrathoracic extension. The largest nodule measured 4.5 cm x 3.5 cm x 5.0 cm with a few punctuate foci suggestive of phleboliths. The right hemithorax showed multiple tortuous vessels within subcutaneous nodules adjoining the abovementioned lesions.

Colonoscopy revealed multiple variably sized (largest lesion 1.2 X 1.0 cms) bluish colored vascular masses with irregular friable surface in the jejunum and ileum.

A biopsy and histopathological evaluation was not undertaken because of the classical morphology and parental refusal.

The Computed Tomography scan of head, upper GI endoscopy, fundoscopy, and abdominal ultrasound studies failed to reveal any abnormality.

The patient was started on oral iron supplements for anemia and asked to report back in case of any bleeding per rectum. For cutaneous lesions, given the larger size, multiplicity, and nature of lesions, patient was referred to the plastic surgery department for excision and reconstructive surgery because sclerotherapy and cryotherapy was not feasible.

The patient and parents were counselled about the possibility of sudden onset hematemesis, rectal bleeding, severe headache, breathlessness, and unremitting musculoskeletal pain as well as the need to continue iron supplementation and regular followup visits. They were also appraised about the genetic aspect of the disease and a possibility of transmission to her children.



Figure 3. Lateral view of the right back showing macular lesions extending up to back. **Figure 4.** Front view thorax showing visible asymmetry on right side

Discussion

BRBNS is a rare disorder characterized classically by cutaneous and visceral, mostly gastrointestinal, vascular malformations, arising at birth or childhood and gradually progressing with age. The same spectrum of findings was seen in our case.

Skin lesions may occur anywhere on body but a predisposition for trunk and extremities has been noted, with association of hyperhidrosis and nocturnal pain over lesions [1]. Our case also had extensive lesions on trunk with pain more frequently experienced at night.

Three distinct types of lesions have been described in Bean's original work [3] and an individual patient may show one or more type of lesions, as in our case in which both nodular blood filled sacs and flat macular lesions were coexistent.

The other hallmark of BRBNS is gastrointestinal vascular malformations present anywhere from oral to rectal mucosa, though more frequently in small intestine [8]. These are quite prone to bleeding, owing to their friability, resulting in anemia. Serious GI bleeding and consumptive coagulopathy with shock can occur [9]. Our patient also had occult blood loss resulting in anemia, which correlated with the colonoscopic findings of venous malformations in jejunum and ileum.

The malformations may be rarely seen in multiple other visceral sites such as brain, pharynx, eye, lung, pleura, heart, peritoneum, liver, spleen, urinary bladder, and uterus [10]. Complications include intracranial hemorrhage, hemothorax, or even airway compromise as in patient described by Gascoyen [2]. Orthopedic deformities and pathological fractures may occur. However, a battery of investigations undertaken in our case failed to reveal abnormalities in other organs.

Histological evaluation of BRBNS lesions reveals ectatic vascular channels lined by a single layer of cuboidal or flattened epithelium surrounded by fibromuscular wall. The differential diagnosis of BRBNS includes multiple hemangiomas,

glomangiomas, hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber syndrome), Maffucci syndrome, Klippel-Trenaunay-Weber syndrome, Sturge-Weber syndrome, and Kaposi sarcoma, which were ruled out owing to typical morphology of cutaneous lesions and associated gastrointestinal lesions.

Cutaneous lesions are not treated unless cosmetically disfiguring or disabling. Sclerotherapy with absolute alcohol/Polidocanol [11], cryotherapy, and carbon dioxide laser ablation are the treatment modalities usually chosen for skin lesions [12]. This, however, was not advised in our patient owing to larger size, multiple lesions, and the presence of lesions on the trunk, which increased the chances of systemic complications.

The GI lesions are mostly treated conservatively with hematinics or blood transfusion to correct anemia and sometimes somatostatin analogues e.g. octreotide or sirolimus, to control bleeding episodes [13]. A surgical intervention with resection/banding is resorted to in cases with troublesome bleeding or severe anemia not responding to medical therapy. Malignant transformation of the lesions has not been reported so far.

The genetic defect in BRBNS is yet to be delineated [5, 6] and there is a need for genetic studies in this regard, to ascertain whether it is the chromosome 9p [7] or any other gene locus responsible for the syndrome. Most of the cases described in literature are sporadic and believed to be related to somatic mutations. The occurrence of disease in an autosomal dominant pattern in a few families [7] mandates the search for other affected family members and genetic counselling.

Although originally described by Bean as nevi [3], the recent studies [7] have suggested that the lesions resemble vascular malformations in their biological behavior. Hence, it is recommended that a change in nomenclature should perhaps be considered for this entity.

In conclusion, a diagnosis of lesions suggestive of BRBNS should alert a busy consulting dermatologist to suspect gastrointestinal and other visceral involvement and undertake investigations to identify these.

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